

## *Covid-19 And Jaundice In Infants*

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**Abstract** – In Tbilisi State Medical University First University Clinic Department of Perinatology, within a framework of retrospective study, the medical histories of 23 pregnant women in 2022 (infected with Sars-CoV-2 at different stages of pregnancy and childbirth) and their newborns were studied which are transferred in the Neonatal Intensive Care Unit (NICU), due to jaundice, for the phototherapy and further monitoring of bilirubin level. As it was determined by data analysis, in 17 out of 23 cases, SARS-CoV-2 infection during pregnancy and childbirth were characterized by a moderate or severe duration of infection, and their newborns were diagnosed with jaundice with an unspecified cause.

Based on our study, it can be assumed that jaundice in newborns, which appeared due to hyperbilirubinemia is a neonatal consequence of SARS-CoV-2, which probably cause placental vascular malperfusion and polycythemia in fetuses, which may be a compensatory response to this infection.

**Keywords** – COVID-19, SARS-CoV-2, NICU, Jundice.

### I. INTRODUCTION

The infection caused by the novel coronavirus Sars-CoV-2 is an RNA virus that first appeared in the Chinese city of Wuhan in December 2019 and has killed more than 6,900,000 people worldwide (1). It is known that COVID-19 infection during pregnancy is associated with increased risks of stillbirth, small for-gestational age fetuses and preterm birth.(2)

In cases of infection confirmed by PCR (polymerase chain reaction) or antigen test in pregnant women, respiratory failure, respiratory distress syndrome, nutritional problems, etc. are mostly expressed in newborns. In this regard, the hyperbilirubinemia of newborns, a clinical problem that manifests itself during the first week of life of newborns, is interesting. Almost 8%-11% of newborns develop hyperbilirubinemia, which means that the total serum bilirubin exceeds the acceptable level, which is determined by the risk factor and indicator during the first week of life.

In newborns, icterus of the skin is first appeared on the face, and as the bilirubin level increases, it spreads to the whole body, and then to the limbs. Appears during the first 24 hours of life or after 7 days of life, the rate of increase of total bilirubin in the blood serum is more than 3.5  $\mu\text{mol/L}$ , total bilirubin is more than 85  $\mu\text{mol/L}$  on the first day of life.(3)

High levels of bilirubin are toxic to the developing central nervous system of newborns and can cause behavioral and neurological complications. Bilirubin is a potential neurotoxin, unconjugated bilirubin can cross the blood-brain barrier and cause brain cell death by apoptosis and/or bilirubin-induced neurological dysfunction (BIND–bilirubin induced neurological dysfunction), including acute and chronic bilirubin encephalopathy (ABE and CBE, respectively), as well as more severe neurological dysfunction. Severe neonatal hyperbilirubinemia is defined as a TSB greater than 25 mg/dL (428 micromol/L), at which time there is a high risk of developing bilirubin toxicity, which is variable and depends on risk factors.(4) The well-

known, main reasons for the increase in the amount of bilirubin in newborns are: increased hemolysis of erythrocytes and a decrease in the ability of bilirubin conjugation.(5)

Pathological jaundice can develop in the following cases: ABO and Rh

Incompatibility, membrane, enzyme, hemoglobinopathies, polycythemia, infection, prematurity, congenital diseases (Crigler-Nayar, Gilbert, Dubin-Johnson), asphyxia, feeding problems, obstruction of meconium passage, intestinal obstruction, etc.(6)

According to the American Academy of Pediatrics (AAP) Clinical Practice Guidelines, the 2022 guidelines recognize the following major risk factors for the development of progressive or severe hyperbilirubinemia:

Table 1.

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1. Jaundice in the first 24 hours of life.
  2. TcB/TSB level is close to phototherapy rate
  3. Hemolysis for any reason or probable hourly increase  $>0.3$  mg/dL in the first 24 hours and  $>0.2$  mg/dL after 24 hours
  4. Phototherapy before discharge from the clinic
  5. Family history of phototherapy, replacement hemotransfusion
  6. Family history, genetic diseases, including G6PD deficiency
  7. Suboptimal breastfeeding
  8. Cephalohematomas and other complications during delivery
  9. Down syndrome
  10. Diabetic fetopathy
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## II. RESEARCH MATERIAL AND METHODS

A retrospective, cohort, targeted study was conducted in the Perinatology Department of the First University Clinic of Tbilisi State Medical University. In 2022, in the Department of Perinatology of our clinic, pregnant women and women in labor with new coronavirus infection (23 pregnant women and women in labor in different trimesters of pregnancy and with different severity) were studied, Also the medical histories of their neonates admitted to the neonatal intensive care unit for hyperbilirubinemia (23 neonates) who required phototherapy and follow-up of bilirubin levels.

## III. RESULTS

Through the analysis of the mentioned material, it was established that the mothers of newborns with hyperbilirubinemia were diagnosed with the new coronavirus disease at different stages of pregnancy or during childbirth, namely: in these pregnant women, the infection was not diagnosed in the 1st trimester. In the second trimester of pregnancy, 23 out of 52.1% of the new coronavirus infections were confirmed by antigen test (21-28 weeks), in the third trimester 6 cases were diagnosed - 26.0% (30-36 weeks), 5 cases were confirmed by the antigen test during delivery, 21.7% (38 -41 weeks) terms, In 5 (21.7%) cases, COVID-19 was asymptomatic - in cases of infection confirmed by an antigen test, no clinical symptoms were detected. n=4 of 23 women (17.4%) cases were characterized by a mild course, in particular,

pregnant women had fever, cough, fatigue, myalgia, as well as other non-specific symptoms, such as sore throat, nasal congestion, headache, diarrhea, nausea and vomiting, anosmia or agosia.

COVID-19 was of moderate duration in n=9 (39.1%) cases, namely with clinical signs of pneumonia (fever, cough, shortness of breath, tachypnea), although there were no signs of severe pneumonia. n=5 (21.7%) cases had a severe duration with clinical signs of pneumonia: fever, cough, shortness of breath, respiratory rate >30 breaths/min.

Analyzing the mentioned data, it was determined that jaundice and hyperbilirubinemia was detected in newborns from mothers, during the moderate and severe duration of the COVID-19 infection, which became the reason for their transfer to the intensive care unit for phototherapy and monitoring of bilirubin levels.

The characteristics of the course of the novel coronavirus infection according to the degree of severity in pregnant women whose newborns were transferred to the neonatal intensive care unit for phototherapy and follow-up due to hyperbilirubinemia are presented in Table N2.

Figure N2

Asymptomatic New coronavirus infection (n=5)	Clinical symptoms were not detected in the cases confirmed by the antigen test
Mild New coronavirus infection (n=4)	Have fever, cough, fatigue, myalgia, non-specific symptoms: sore throat, nasal congestion, headache, diarrhea, nausea and vomiting, anosmia or agesia
Moderate new coronavirus infection (n=9)	Clinical signs of pneumonia: fever, cough, shortness of breath, shortness of breath, although there were no signs of severe pneumonia
severe New coronavirus infection (n=5)	With clinical signs of pneumonia (fever, cough, shortness of breath, tachypnea). Breathing rate > 30 breaths/min

In 2022, in the Department of Perinatology of the First University Clinic of TSU, out of 94 newborns who were transferred to the neonatal intensive care unit, n=23 (24.46%) developed hyperbilirubinemia and required phototherapy and further monitoring of bilirubin levels, of which n=2 (8.7%) were shortness of breath In n=2 (8.7%) cases, incompatibility with the ABO system was observed, in n=1 (4.34%) case, Rh incompatibility, in n=1 (4.34%) case, cephalohematoma developed during childbirth, in n=17 (73.9%) cases, hyperbilirubinemia developed for an unspecified reason was noted. (no risk factors were identified)

As determined by the data analysis, in the case of the mentioned (n=17) pregnant and parturient women, there was a moderate or severe course of the novel coronavirus infection and their correlation with hyperbilirubinemia in newborns, which was detected in the less than 24 hours after birth and was on average  $\geq 205 \mu\text{mol/L}$ .

#### IV. CONCLUSION

Thus, on the basis of our study, it is possible to assume that jaundice and hyperbilirubinemia is one of the neonatal outcomes during moderate and severe course of SARS-CoV-2 infection in mothers. Sars-CoV2 infection can cause placental vascular malperfusion, likely leading to polycythemia in fetuses as a compensatory response, possibly representing a link between maternal COVID-19 and neonatal

#### REFERENCES

- [1]. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020; (published online Jan 24. [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5).)
- [2]. Ronald J Wong, BA, Vinod K Bhutani, MD, FAAP, Unconjugated hyperbilirubinemia in neonates: Risk factors, clinical manifestations, and neurologic complications
- [3]. Bhutani VK, Johnson L, Sivieri EM. , Predictive ability of a predischarge hour-specific serum bilirubin for subsequent significant hyperbilirubinemia in healthy term and near-term newborns. *Pediatrics*. 1999;103:6–14. doi: 10.1542/peds.103.1.6.
- [4]. Association Between COVID-19 Pregnant Women Symptoms Severity and Placental Morphologic Features. Rebutini PZ, Zanchettin AC, Stonoga ETS, Prá DMM, de Oliveira ALP, Dezielério FDS, Fonseca AS, Dagostini JCH, Hlatchuk EC, Furuie IN, Longo JDS, Cavalli BM, Dino CLT, Dias VMCH, Percicote AP, Nogueira MB, Raboni SM, de Carvalho NS, Machado-Souza C, de Noronha L. *Front Immunol*. 2021 May 26;12:685919. doi: 10.3389/fimmu.2021.685919. eCollection 2021. PMID: 34122449